Methods

- **Study Design and Population.** A clinical algorithm for CYP2C19 genotype-guided selection of antiplatelet therapy following PCI in high-risk patients (defined as ACS and/or major risk coronary anatomy) was implemented at the University of North Carolina (UNC) Cardiac Catheterization Laboratory in July 2012.(12) The CYP2C19 genotype test is ordered at the interventional cardiologist’s discretion following risk stratification, and performed clinically on-site. Alternative antiplatelet therapy (prasugrel or ticagrelor) is recommended for CYP2C19 IMs and PMs, but the treatment decision is left to the discretion of the prescriber.

- **Data Abstraction.** Data was manually abstracted from the electronic health record (EHR).

- **Clinical Endpoints.** The primary clinical endpoints were major diverse cardiovascular or cerebrovascular events (MACCE) and clinically significant bleeding. MACCE were defined as death, myocardial infarction, stent thrombosis, admission for ACS/unsustainable angina, ischemic cerebrovascular accident (CVA), or transient ischemic attack (TIA). Clinically significant bleeding was defined as a Global Use of Strategies to Open Occluded Arteries (GUSTO) moderate or severe/life-threatening bleeding event.(19)

- **Statistical Analysis.** Cox proportional hazards regression and Kaplan-Meier event curves were used to evaluate the relationship between CYP2C19 status, prescribed P2Y12 inhibitor therapy, and the time to occurrence of the primary (MACCE) and secondary (clinically significant bleeding) clinical outcomes in patients with follow-up available after the index PCI admission. Secondary analyses were completed in the strata of patients presenting with an ACS indication for their PCI.

Results

![Figure 1 - Clodiregol vs. Alternative Therapy in the Total Population](image1)

- MACCE occurred in 124 patients (13.3%) while a clinically significant bleed occurred in 41 patients (4.4%) during the study period.
- In 17 carriers, there was no difference in the incidence of MACCE treated with clopidogrel vs. alternative therapy.
- Patients with an LOF mutation were 3.4X more likely to have a MACCE while Extensive Metabolizers (EM) were 1.7X more likely if prescribed clopidogrel.
- No significant statistical differences were noted when considering the relative risk of having a bleeding event between clopidogrel vs. alternative therapy in ACS patients with IM/PM, EM, or UMR phenotype.

![Figure 2 - Clodiregol vs. Alternative Therapy in the ACS Population](image2)

- The study population included 569 patients (61.3%) with ACS including 329 patients treated with clopidogrel and 240 patients on alternative therapy. There was no difference in MACCE or clinically significant bleeding events between UMR treated with clopidogrel vs patients on alternative therapy.
- Similar to the total population IM/PM patients with an ACS indication also exhibited higher rates of MACCE on clopidogrel vs. alternative therapy.
- The incidence of moderate or severe bleeding events was similar in all groups irrespective of treatment (clopidogrel vs. alternative therapy) or phenotype.

![Figure 3 - Clodiregol vs. Alternative Therapy in UMR/PM Population](image3)

- There were 173 UMR patients treated with clopidogrel and 68 UMR patients treated with alternative therapy.
- There was no difference in the incidence of MACCE between UMR/PM patients treated with clopidogrel vs alternative therapy.
- UMR/PM patients exhibited statistically equivalent incidences of major bleeding events, regardless of treatment with clopidogrel or alternative therapy.
- The incidence of combined MACCE and major bleeding events was similar within the UMR/PM population between those treated with clopidogrel vs. alternative therapy.

References